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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/759,803	01/16/2004	Daniel E. Afar	511582001310	8272
25225	7590	07/12/2005	EXAMINER	
MORRISON & FOERSTER LLP 3811 VALLEY CENTRE DRIVE SUITE 500 SAN DIEGO, CA 92130-2332			TUNGATURTHI, PARITHOSH K	
			ART UNIT	PAPER NUMBER
			1643	

DATE MAILED: 07/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/759,803

Applicant(s)

AFAR ET AL.

Examiner

Parithosh K. Tungaturthi

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on January 16, 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 38 and 39 is/are pending in the application.
- 4a) Of the above claim(s) 39 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 38 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 04.11.2005.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

5.00

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:
 - I. Claim 38, drawn to a vaccine composition for the treatment of a cancer expressing 30P3C8 comprising an immunogenic portion of a 30P3C8 polypeptide and a physiologically acceptable carrier, classified in class 514, subclass 2-21.
 - II. Claim 39, drawn to a method of inhibiting the development of a cancer expressing 30P3C8 in a patient, comprising administering to the patient effective amount of the vaccine, classified in class 514, subclass 2.
2. The inventions are distinct, each from the other because of the following reasons:

The inventions of Group I and the method of Group II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (i) the process for using the product as claimed can be practiced with another materially different product or (ii) the product as claimed can be used in a materially different process of using that product [see *MPEP* § 806.05(h)]. In the instant case the polypeptide as claimed can be used in a materially different process such as antibody production in addition to the materially different methods of Groups II.

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3. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper. Furthermore, because these inventions are distinct for the reasons given above and the search required for one group is not required for another group, restriction for examination purposes as indicated is proper.

4. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. Process claims that depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims

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and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. Failure to do so may result in a loss of the right to rejoinder. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

6. During a telephone conversation with Ms. Carolyn Favorito on ⁰⁶~~07~~.21.2005 a provisional election was made without traverse to prosecute the invention of Group I, claim 38. Affirmation of this election must be made by applicant in replying to this Office

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action. Claim 39 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

7. Claim 38 is pending and is currently under consideration

Specification

8. The disclosure is objected to because of the following informalities: The first line of the specification states that instant application claims priority to U.S. Application Serial No. 09/547,788; which is now abandoned, and thus needs to be updated.

Appropriate correction is required.

9. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (page 12, line 23; page 30, lines 7-8). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

10. The use of the trademark HERCEPTIN (page 51, line 28) has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claim 38 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 38 is drawn to a vaccine composition for the treatment of a cancer comprising an immunogenic portion of a polypeptide and a physiologically acceptable carrier. However, the specification provides insufficient guidance and objective evidence that such pharmaceutical compositions and or vaccines formulations would predictably invoke an anticancer or immunotherapeutic response. The specification provides no guidance on the administration of the claimed complex or any portion thereof in vivo or in vitro.

UNDUE EXPERIMENTATION

The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 USPQ 1165, 1174 (Int'l Trade Comm'n 1983), *aff'd sub nom., Massachusetts Institute of Technology v. A.B. Fortia*, 774 F. 2d 1104, 227 USPQ 428 (Fed. Cir. 1985). See also *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. The test enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue, *In re Angstadt*, 537 F. 2d 498, 504, 190 USPQ 214, 219 (CCPA 1976).

2164.01(a) Undue Experimentation Factors

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include, but are not limited to:

- (A) The breadth of the claims
- (B) The nature of the invention
- (C) The state of the prior art
- (D) The level of one of ordinary skill
- (E) The level of predictability in the art
- (F) The amount of direction provided by the inventor
- (G) The existence of working examples; and
- (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

In re Wands, 88 F.2d at 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (reversing the PTO's determination that claims directed to methods for detection of hepatitis B surface antigens did not satisfy the enablement requirement). In *Wands*, the court noted that there was no disagreement as to the facts, but merely a disagreement as to the interpretation of the data and the conclusion to be made from the facts. *In re Wands*, 858 F.2d at 736-40, 8 USPQ2d at 1403-07. The Court held that the specification was enabling with respect to the claims at issue and found that "there was considerable direction and guidance" in the specification; there was "a high level of skill in the art at the time the application was filed;" and "all of the methods needed to practice the invention were well known." 858 F.2d at 740, 8USPQ2d at 1406. After considering all the factors related to the enablement to obtain antibodies needed to practice the claimed invention. *Id.*, 8 USPQ2d at 1407.

In general, the treatment of cancer is at most unpredictable as underscored by Bodey et al (Anticancer Research. 20:2665-2676; 2000) who discusses the potential shortcomings of potential anti-cancer agents including conventional surgery, radiation and chemotherapies. The cancer vaccine approach to therapy is based on the notion that the immune system could possibly mount a rejection strength response against the neoplastically transformed cell conglomerate. However, due to the low immunogenicity of the tumor associated antigens (TAAs), downregulation of MHC molecules, the lack of adequate costimulatory cytokines, etc., such expectations are rarely fulfilled. Various approaches have been explored ranging from the use of irradiation inactivated whole-cell vaccines derived from both autologous and allogenic tumors (even tumor cell lines),

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and genetically modified versions of such cellular vaccines which aim at correcting costimulatory dysfunction or altering the in situ humoral milieu to aid immune recognition and activation. Anti-idiotypic vaccines, based on cancer cell associated idiotypes, have also been explored which aim at increasing immunogenicity through in vivo generation of vigorous immune responses. Dendritic cell vaccines seek to improve the presentation of TAAs to naïve T lymphocytes. Unfortunately, there is always the possibility of faulty antigen presentation which could result in tolerance induction to the antigens contained within the vaccine, and subsequent rapid tumor progression (see abstract, in particular). Further, Bellone *et al* (Immunology Today, v20 (10), 1999, pp.457-462) summarize the current state of the art of peptide immunotherapy including clinical trials where "there is usually a poor correlation between induction of specific T-cells and the clinical responses" (page 457, 2nd column). Bellone *et al.* teach the disadvantages of peptide cancer immunotherapy in that (1) there is no direct evidence for a role in tumor rejection, (2) the therapy is applicable to few patients, (3) risk of generating tumor escape mutants, and (4) risk of autoimmune reactions (page 461, Box 1). Indeed, Gaiger *et al.* (Blood, Volume 96, No. 4, August 2000, pages 1480-1489) chose to evaluate the Wilm's tumor antigen (WT1) as a potential immunotherapeutic as it is well known in the art that WT1 protein expression is more abundant in leukemia cells than in normal hematopoietic cells. However, WT1 peptide immunization did not show any effect on tumor growth in-vivo (Figure 10, page 1486). All of this underscores the criticality of providing workable examples which is not disclosed in the specification, particularly in an unpredictable art, such as cancer therapy.

In view of the teachings above, and the lack of guidance and or exemplification in the specification, at the time the application was filed it would not have been predictable for of skill in the art to use the pharmaceutical compositions or vaccine formulations as contemplated in the disclosure. Thus, it would require undue experimentation by one of skill in the art to practice the invention as claimed.

2. Claim 38 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 38 is drawn to a vaccine composition comprising an immunogenic portion of 30P3C8 polypeptide. The specification describes term "30P3C8" as a fusion protein that combine part of different 30P3C8 proteins or fragments thereof, as well as fusion proteins of a 30P3C8 protein, including heterologous polypeptides (page 24, lines 5-10). The claim does not require any particular limitation of the polypeptide excluding the immunogenic portion of the polypeptide. Thus, the claim is drawn to a genus of polypeptides that is defined by only by the term "30P3C8".

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial

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structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

In this case, the only factor present in the claim is in the form of a recitation of "30P3C8" and is defined as amino acid sequence, but will further contain a radical departure from the sequence, such a 90% or more identity, non-conservative substitution, truncation, insertion or frame shift (page 24, lines 18-26). There is not even identification of any particular portion of the structure that must be conserved or is responsible for a "30P3C8" polypeptide. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. The only species is SEQ ID NO:2.

Vas-cath Inc. F. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that (he or she) invented what is claimed." (See *Vas-cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The

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compound itself is required. See *Fiers k: Revel*, 25 USPQZd 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQZd 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQZd 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF'S were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only amino acid set forth in SEQ ID NO: 2 but not the full breadth of the claim meets the written description provision of 35 U.S.C. 112, first paragraph. Applicant is reminded that *Vas-cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

13. Claim 38 is rejected under 35 U.S.C. 102(e) as being anticipated by Baker et al (U.S. Patent application publication 2003/0077712, with priority to 10/98; IDS – April 11th, 2005).

The claim is drawn to a vaccine composition for the treatment of a cancer expressing 30P3C8 comprising an immunogenic portion of a 30P3C8 polypeptide and a physiologically acceptable carrier. As disclosed in the instant specification, the 30P3C8 polypeptide comprises of SEQ ID NO:2.

In response to "a vaccine composition for the treatment of a cancer expressing 30P3C8 comprising an immunogenic portion of a 30P3C8 polypeptide and a physiologically acceptable carrier", a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 370 F.2d 576, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 312 F.2d 937, 939, 136 USPQ 458, 459 (CCPA 1963).

For this rejection, the recitation "for the treatment of a cancer" and "vaccine" has not been given patentable weight.

Baker et al teach a polypeptide that is identical to SEQ ID NO:2 (see SEQ ID NO: 486 in Baker et al). Baker et al also teach a composition comprising the polypeptide, or an agonist, or antagonist, in combination with a pharmaceutically acceptable carrier (page 5, lines 30-32). Further, since the claim recites "immunogenic portions" and Baker et al teach the antibodies that bind to the polypeptide (SEQ ID 486) identical to SEQ ID NO:2, it is inherent that the polypeptide taught by Baker et al consists of the "immunogenic portions" within itself. Since, the instant claim is drawn to a composition

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"comprising" the immunogenic portion of the polypeptide and Baker et al teach a composition consisting of the entire length of an identical polypeptide, it would be inherent that Baker et al would have the claimed composition therefore meeting the limitation of claim 38.

Conclusions

14. No claims are allowed

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Parithosh K. Tungaturthi whose telephone number is 571-272-8789. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-~~703-~~

273-8300

~~872-9300~~.



LARRY R. HELMS, PH.D.
PRIMARY EXAMINER

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16. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
Parithosh K. Tungaturthi Ph.D.
(571) 272-8789